IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Heeney, et al
Serial No.:	10/502,031
Filed:	July 20, 2004
For:	Treatment of MS with Goat Serum
Group:	Unassigned
Examiner:	Unassigned

Commissioner for Patents
Box 1450
Alexandria, VA 22313-1450

RENEWED PETITION UNDER 37 CFR 1.137(b) AND 37 CFR 1.47(a)

Sir:

This is a renewed petition under 37 CFR 1.137(b) and 37 CFR 1.47(a), to revive the above-identified application on the grounds that the abandonment of the above-identified application was unintentional, and to accept the above-identified application without the signature of one of the inventors, Jonathan Heeney, in response to the Decision mailed July 22, 2010.

Accompan ying this renewed petition is a Declaration of Gareth Williams. Mr. Williams is a Chartered Patent Attorney and a European Patent Attorney in the United Kingdom with the firm of Marks & Clerk. Marks & Clerk filed the corresponding PCT Application No. PCT/GB03/00342.

Mr. Williams testified that he sent a Declaration and Power of Attorney, and a copy of PCT Application No. PCT/GB03/00342, to Jonathan Heeney at his last known address, i.e.,

Vrijburgstraat 25, Voorburg, 2275BX, The Netherlands, on August 17, 2010. Mr. Williams was informed of Mr. Heeney's last known address through previous correspondence with Mr. Heeney's legal representatives, HGF Law with respect to another application that included Mr. Heeney as a co-inventor, i.e., Application Serial No. 10/482,399.

The firm of Marks & Clerk received a signed receipt as confirmation that the Declaration and Power of Attorney, and a copy of PCT Application No. PCT/GB03/00342, sent on August 17, 2010, had been delivered to Mr. Heeney.

Mr. Williams then testifies that, to the present date, he has received no response from Mr. Heeney.

Thus, a declaration and power of attorney, and a copy of the above-identified application, were sent to Mr. Heeney at his last known address. Mr. Heeney received the Declaration and Power of Attorney and the application; however, he has not signed the Declaration and Power of Attorney, nor has he responded to Mr. Williams. Therefore, it can be concluded that Mr. Heeney is refusing to sign the Declaration and Power of Attorney after he had been provided with the Declaration and Power of Attorney and a copy of the application at his last known address. It is therefore respectfully requested that the Renewed Petition Under 37 CFR 1.137(b) and 37 CFR 1.47(a) be granted, that the above-identified application be revived, and that the above-identified application be accepted without the signature of Jonathan Heeney.

Respectfully submitted,

Raymond J. Lillie

Raymond J. Lillie
Registration No. 31,778

#403478 v1

IN RESPECT OF US
PATENT APPLICATION
10/502,031

DECLARATION

I, Gareth Williams, of Marks & Clerk LLP, 62-68 Hills Road, Cambridge CB2 1LA, United Kingdom, declare as follows.

1. I am a Chartered Patent Attorney and European Patent Attorney, and practise in the UK.

2. International Patent Application PCT/GB03/00342 was filed by Marks & Clerk on behalf of Aimsco Limited, naming three inventors: Angus G Dalgleish, Jonathan Heeney and Stanley D T White.

3. On 17 August 2010, I sent a copy of International Patent Application PCT/GB03/00342 and a Declaration of Inventorship document to Jonathan Heeney at his last known address at Vrijburgstraat 25, Voorburg, 2275 BX, the Netherlands. A copy of the letter sent to Jonathan Heeney is attached as Annex I.

4. We obtained a signed receipt as confirmation that this document had been delivered and received at the above address. A copy of this document is attached as Annex II.

5. I have had similar problems obtaining a signature from Jonathan Heeney for another U.S. application, also filed on behalf of Aimsco Ltd. This application is U.S. Patent Application No. 10/482,399 (International Patent Application PCT/GB02/03037).

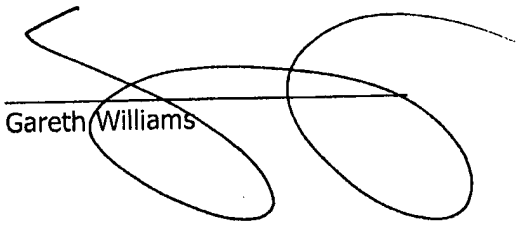
6. On 10 June 2008, I sent a copy of International Patent Application PCT/GB02/03037 and a Declaration of Inventorship document to Jonathan Heeney at his academic address at the Department of Veterinary Medicine, Madingley Road, Cambridge, United Kingdom.

7. In response to our 10 June 2008 letter, we received a response from HGF Law, who are the legal representatives of Jonathan Heeney for both applications. A copy of this letter is also attached as Annex III. This letter stated that all correspondence to Jonathan Heeney should to be sent to his address in the Netherlands. For this reason on 17 August 2010 we sent the application and Declaration of Inventorship documents for this application to Jonathan Heeney at his address in the Netherlands.

8. The letter from HGF law also made reference to an earlier letter dated 5 April 2007, in which HGF law stated that Jonathan Heeney would be prepared to sign on the basis that all monies owed to him are paid and on the basis that all claims against Jonathan Heeney are withdrawn. A copy of this letter is enclosed as Annex IV.

9.To date, I have received no response from Jonathan Heeney.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like are punishable by fine or imprisonment, or both, under 18 USC 1001 and that such wilful false statements may jeopardise the validity of the application or any patent issued thereon.



Gareth Williams

20 September 2010

ANNEX I

Marks&Clerk LLP
Patent and Trade Mark Attorneys

Cambridge Office
62-68 Hills Road, Cambridge CB2 1LA
Tel: +44 (0)1223 345520 Fax: +44 (0)1223 365560
cambridge@marks-clerk.com www.marks-clerk.com

Jonathan Heeney
Vrijburgstraat 25
Voorburg, 2275 BX
Netherlands

Our Ref: GOW/aw/PC760077US

Your Ref:

Date: 17 August 2010

By Courier

Dear Dr Heeney

Re: United States Patent Application No 10/502,031
In the name of AIMSCO Limited

In connection with the above-referenced application, we enclose a copy of International Patent Application No.PCT/GB2003/00342, which has now entered the U.S. national, phase as U.S. Patent Application No.10/502,031, and a Declaration of Inventorship document. You are named as an inventor of this patent application, and for it to proceed, the U.S. Patent Office requires the completed Declaration from you.

We have been informed by Harrison Goddard Foote, who we understand are your representatives, that the above address is the correct address at which to contact you.

We would be grateful if you could sign the Declaration and return it to us at your earliest convenience.

If you do not intend to sign the Declaration, I would be grateful if you could confirm this to me by return.

Yours sincerely

Gareth Williams
for MARKS & CLERK LLP

Enc. Declaration of Inventorship
PCT application: PCT/GB02/03037

DECLARATION AND POWER OF ATTORNEY

As a below named inventor I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

TREATMENT OF MS WITH GOAT SERUM

the specification of which ☒ is attached hereto or ☐ was filed on _____ as Application Serial No. _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability of this application in accordance with Title 37 Code of Federal Regulations Section 1.56(a).

I hereby claim foreign priority benefits under Title 35 United States Code Section 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed. Prior Foreign Application(s):

			Priority Claimed	
			Yes	No
PCT/GB02/03037 (Number)	PCT (Country)	2 July 2002 (Day/Month/Year Filed)	☒	☐
0201896.8 (Number)	United Kingdom (Country)	28 January 2002 (Day/Month/Year Filed)	☒	☐

I hereby claim the benefit under Title 35 United States Code Section(s) 119 and/or 120 of any United States application(s) listed below and insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35 United States Code Section 112 I acknowledge the duty to disclose material information as defined in Title 37 Code of Federal Regulations Section 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

PCT/GB03/00342 (Application Serial No.)	January 28, 2003 (Filing Date)	Pending (Status – pending provisional, patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status – pending provisional, patented, pending, abandoned)

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: John N. Bain (Reg. No. 18,651); John G. Gilfillan, III (Reg. No. 22,746); Elliot M. Olstein (Reg. No. 24,025); Raymond J. Lillie (Reg. No. 31,778); William Squire (Reg. No. 25,378); Alan J. Grant (Reg. No. 33,389); Francis C. Hand (Reg. No. 22,280); Glennon G. Troublefield (Reg. No..39,050); Raymond E. Stauffer (Reg. No. 47,109), and Michael A. Petrocelli (Reg. No. 53,461). Address correspondence and telephone calls to Raymond J. Lillie, Esq., c/o Carella, Byrne, Bain, Gilfillan, Cecchi, Stewart & Olstein, 5 Becker Farm Road, Roseland, NJ 07068 - (973) 994-1700.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor: Jonathan Heeney

Inventor's signature _____ Date _____

Residence _____ Citizenship Canada

Post Office Address Vrijburgstraat 25

2275 BX Voorburg, Netherlands

Full name of second inventor: Angus George Dalgleish

Inventor's signature _____ Date _____

Residence _____ Citizenship United Kingdom

Post Office Address 7 Burdon Lane
Cheam
Surrey Su12 7PP
United Kingdom

Full name of sole third inventor: Stanley D.T. White

Inventor's signature _____ Date _____

Residence _____ Citizenship U.S.A.

Post Office Address 315 Czeski Road
P.O. Box 326
Hardwick, Massachusetts 01037

#226921 v1
430500-11

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 August 2003 (07.08.2003)

PCT

(10) International Publication Number
WO 03/064472 A2

(51) International Patent Classification[7]: C07K 16/00

(21) International Application Number: PCT/GB03/00342

(22) International Filing Date: 28 January 2003 (28.01.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0201896.8 28 January 2002 (28.01.2002) GB
PCT/GB02/03037 2 July 2002 (02.07.2002) GB

(71) Applicant *(for all designated States except US)*: **AIMSCO LIMITED** [GB/GB]; 4a Gildredge Road, Eastbourne, East Sussex BN21 4RL (GB).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **HEENEY, Jonathan** [CA/NL]; Vrijburgstraat 25, NL-2275 BX Voorburg (NL). **DALGLEISH, Angus, G.** [GB/GB]; 7 Burdon Lane, Cheam, Surrey SU12 7PP (GB). **WHITE, Stanley, D., T.** [US/US]; P.O. Box 236, 315 Czeski Road, Hardwick, MA 01037 (US).

(74) Agent: **RUFFLES, Graham, Keith**; Marks & Clerk, 57-60 Lincoln's Inn Fields, London WC2A 3LS (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/064472 A2

(54) Title: TREATMENT

(57) Abstract: A serum composition from a goat immunised with HIV contains anti-HLA antibody and is suited for palliative improvement of the condition of an animal.

Treatment

The present invention relates to a treatment.

BACKGROUND OF THE INVENTION

WO 97/02839 relates to Viral Suppression, Treatment and Prevention of Viral Infections. It provides a method for producing neutralizing antibodies for the treatment of a viral infection in a patient, comprising the steps of:

a. exposing a mammal to a virus such that said mammal produces neutralizing antibodies to said virus and

b. collecting said neutralizing antibodies from said mammal.

In the examples, an HIV vaccine designated AAV2 is obtained by mixing HIV virus with HIV neutralizing antibodies obtained from a goat.

WO 01/60156 relates to Neutralizing Antibody and Immunomodulatory Enhancing Compositions. It provides an immunomodulatory composition comprising:

heterologous antibodies specific for an antigen; and

an antigen, wherein the heterologous antibodies form a complex with the antigen for combination with a pharmaceutical carrier.

The examples are similar to those of WO 97/02839, and again an HIV vaccine designated AAV2 is obtained by mixing HIV virus with HIV neutralizing antibodies obtained from a goat.

WO 02/07760 is concerned with a Therapeutic Agent. It provides a method of preventing HIV infection or treating an individual infected with HIV, comprising the steps of

(1) exposure of goat immune system to HIV;
(2) purification of antibody from the goat after HIV challenge; and
(3) treatment of an individual with the antibody obtained in step 2 above.

PCT/GB 02/03037 is concerned with a therapeutic agent, and reports on the discovery of anti-HLA and other antibody activity in a composition prepared from goat serum following HIV challenge. The present PCT application claims priority of PCT/GB 02/03037. We incorporate in full by reference the content of PCT/GB 02/03037.

In preliminary trials based on the product of PCT/GB 02/03037, patients with HIV have been treated successfully using serum from a goat after challenge with HIV.

Preferably the treatment employs a serum composition which can be obtained by a process involving raising effective antibodies in a goat, draining blood from the goat, demonstrating HIV neutralising capability in the drawn blood, removing solids from the blood, precipitating using supersaturated ammonium sulphate or other suitable precipitation agent, separating the precipitate, dissolving the precipitate in a suitable aqueous medium, and dialysing the solution with a cut-off of 5,000 to 50,000 Daltons, preferably 7,000 to 30,000 Daltons, more preferably 8,500 to 15,000 Daltons, especially about 10,000 Daltons. The method of goat immunisation can be intramuscular but other standard techniques such as subcutaneous or intradermal adminstration can also be used. The purification process can also be completed by other commonly used fractionation action methods (caprylic acid for example) provided the total residue is used.

More particularly, the treatment typically employs a goat serum obtained in the following way.

Example of Production of Goat Serum

A goat was inoculated by intramuscular injection with lysed HIV-3b virus suspended in a normal commercial supernate, using an intra-muscular injection of HIV-3b at a concentration of 10^9 viral particles per ml. The virus was previously heat killed at 60°C for 30 minutes. Blood samples were drawn after an appropriate interval, such as two weeks, for initial assessment. In the optimised procedure, the goat is injected every week for four weeks, then at six weeks the animal is then bled to obtain the reagent.

Approximately 400 cc of blood is drawn from the goat under sterile technique. The area for needle extraction is shaved and prepared with betadine. An 18-gage needle is used to draw approximately 400 cc of blood from the animal. Of note is that the animal can tolerate approximately 400 cc of blood drawn without the animal suffering any untoward effects. The animal does not have to be sacrificed. The animal can then be re-bled in approximately 10 to 14 days after it replenishes its blood volume.

The presence of potentially useful antibodies was confirmed. Once the presence of such reagents was confirmed blood was then taken from the goat at between 4-6 weeks, and centrifuged to separate the serum. 300ml of serum was then filtered to remove large clots and particulate matter. The serum was then treated with supersaturated ammonium sulfate (45% solution at room temperature) to precipitate antibodies and other material. The resulting solution was centrifuged at 5000 rpm for five minutes, after which the supernatant fluid was removed. The precipitated immunoglobulin was resuspended in phosphate-buffered saline ('PBS buffer', see Sambrook et. al. 'Molecular cloning, A Laboratory Manual', 1989) sufficient to redissolve the precipitate.

The solution was then dialysed through a membrane with a molecular weight cut off of 10,000 Daltons. Dialysis was carried out in PBS buffer,

changed every four hours over a period of 24 hours. Dialysis was carried out at 4°C.

After 24 hours of dialysis the contents of the dialysis bag were emptied into a sterile beaker. The solution was adjusted such that the mass per unit volume = 10 mg per ml. The dilution was carried out using PBS. The resulting solution was then filtered through a 0.2 micron filter into a sterile container. After filtration, the solution was divided into aliquots to give single doses of 1ml and stored at -22°C prior to use.

The reagent is then ready for use.

Changes may be made in this procedure, such as for example by varying the concentration of the ammonium sulphate or switching to ther reagents. Similarly the dialysis cut-off need not be at 10,000 Daltons.

THE INVENTION

The present invention provides a method for palliation of the condition of a recipient human or non-human animal.

In a related aspect, the invention provides a method for improving the general physical and/or mental condition of a human or non-human animal.

Furthermore, a method of this invention gives treatment to increase well being and/or self-respect.

The invention also provides a procedure for improving quality of life.

In a particular aspect, the conditions to be treated are indicative of, or associated with, the ageing process, or are indicative of health and welfare.

In a related version, we provide a process of rejuvenation. In this respect, we have observed that administration of the product leads to reversal of some body conditions often attributed to old age, such as improved skin elasticity, memory, eyesight. In effect it rejuvenates parts of the body.

In one aspect, the present invention employs a composition containing anti-HLA antibody. In this respect the antibody can be natural or engineered, and can be entire or partial. Thus, for example, the anti-HLA antibody can be a Fab.

In a related aspect, the present invention employs a serum composition obtained from the serum of a goat after challenge with HIV lysate. The composition can be prepared by the method given as an Example of Production of Goat Serum.

Examples of conditions which may be palliatively treated by the present invention include skin, nails, hair, muscles, memory, co-ordination, energy levels, depression, appetite and sexual activity.

In general, administration of the composition to a human or other animal in need can result in a significant improvement in one or more of these conditions. One or more administrations may be given, and typically the benefits are observed after a series of at least three, five or more administrations.

The animal is usually a human who may or may not have some disease or other illness requiring treatment. The illness can be one susceptible to treatment by a composition employed in the present invention.

Thus, the present invention embraces treatment of humans who may or may not be receiving some other treatment apart from the goat serum product, and may or may not have an illness being treated.

Typically the invention employs a composition including the active component which can be derived from the blood of a suitably challenged goat by a serum extraction technique that is not designed to isolate individual, specific antibodies. In particular, the invention envisages isolation of the active component, which we currently believe includes anti-HLA antibody, possibly a mixture of co-operating anti-HLA antibodies and/or FAS antibodies, from blood serum of the challenged goat, without the requirement for exhaustive purification and extraction to obtain an individual antibody. The observed benefits such as on the hair and skin tone and colour, i.e. anti-ageing, suggest unique properties which cannot necessarily be explained exclusively in terms of antibodies.

All of the available data to-date point to the fact that the activity does not stem from an anti-HIV neutralising antibody. Accordingly, in one preferred aspect, we provide a composition, suitably one obtained from a goat after challenge with an immunogen, where the composition does not include anti-HIV neutralising antibody.

Without being bound by any theory or hypothesis, it seems that the working substance may include a biologically active goat molecule that is not a goat antibody, but a cytokine, hormone, or similar type molecule that is retained through the crude purification process.

If the active substance is an antibody then it may be recognising one or more ligands or receptors which *in vivo* are triggering the physiological effects we are observing.

The molecules of interest may or not be shared with the virus from either the H9 lymphoma cell line or activated human PBMCs used to grow the virus. The role of the viral immunogen in this invention is not clear. It may or may not be required. If it is required then it may either induce danger signals in the cells to secrete the molecules of interest, or to bind and transport these molecules (such as HLA, or LFA-1 etc etc) out of the cell into the supernatant.

In general, injection of antibodies or serum compositions into humans derived from a non-human host is counter-indicated. A strong immune response is normally mounted against the foreign antibodies themselves. However, surprisingly, it has been discovered that use of goat serum extract does not provoke the immune reactions which are anticipated with other foreign animal proteins. Injection of goat serum extract is tolerated both by immunosuppressed patients and normal individuals.

The present invention specifically uses a serum extract, which possibly comprises the total population of antibody molecules including anti-HLA activity, derived from HIV challenge to a goat. Without wishing to be constrained by theory, we believe that such an approach possesses significant benefits. Patients treated with such a serum extract showed significant effects within minutes of being treated.

A killed virus is injected into a specifically identified goat, by intra-muscular injection, and allowed to incubate. Thereafter a measured quantity of blood is drawn and modified accordingly.

After inoculation of a selected goat with the HIV virus, an immune response due to exposure to a foreign protein antigen, was noted in accordance with earlier studies. The extracted serum was then further modified in order to prepare it for human use.

Treatment is given by means of a subcutaneous injection, in amounts varying between one/tenth and ten cc and is designed to deliver the medication as speedily as possible to the lymphatic system. With the present invention, the preferred dose is usually 1 ml weekly or as required, given as a divided dose into both arms. Administration every 2 or 3 weeks becomes typical, then every 3 months. For cancer patients, 0.3 ml weekly seems best.

In most cases the treatment has been conducted once ever four weeks over a three month period. General observations are as follows:

1. Moderate to severe depression was reversed in less than sixty minutes post injection.
2. Patients generally within two hours post injection regained their appetites and actively sought out food.
3. Within approximately two weeks of the first treatment the patients started to gain weight.
4. Independent laboratory reports confirmed that 4 to 6 weeks after the first treatment the viral loads and P24 values were dropping substantially and that CD4 and CD8 cells were increasing dramatically.
5. Significant side effects were not observed.

It is important to note that the present medication, unlike current treatments, does not require the patient to maintain a strict hourly or daily regime and relies upon a simple injection being administered either weekly or monthly.

Preferably, the composition is purified and consists essentially only of a purified serum extract. In a further variation, the product may also be purified by conventional or any other suitable procedure, including, but not limited to, for example immunaffinity chromatography, salt precipitation, ion exchange chromatogrpahy, size chromatography, affinity chromatography, in combination as appropriate or desired.

The goat serum extract produced as described herein may be formulated in accordance with the invention in a palliative composition. As such, the invention also relates to pharmaceutical compositions comprising the goat reagent of the present invention, suitable for the treatment. The reagent of the present invention may be mixed with suitable pharmaceutically acceptable carriers.

Examples of pharmaceutical compositions include any solid (tablets, pills, capsules, granules etc.) with suitable composition, or oral, topical or parenteral administration, and they may comprise a carrier. The compositions may need to be sterile when administered parenterally.

A test dose is employed usually to see if the person develops an allergic reaction to the hyperimmune goat serum. An intradermal injection is followed by a wait of 30 minutes to see if there is an intermediate reaction which is manifested as oedema, erythemia, and itching. If this reaction is negative, then the assumption is that an immediate sensitivity reaction is most likely to occur. An allergic reaction does not preclude the person, however, from receiving a potential life-saving treatment because of a possible allergic reaction.

Administration of the composition of the invention may be by any suitable method such as by intravenous infusion, subcutaneously, intra-muscular injection, oral preparation, intraperitoneal and intravenous administration. The correct dosage will vary according to the particular formulation, the mode of application, and the particular situs, host and condition being treated. Other factors like age, body weight, sex, diet, time of administration, rate of excretion, condition of the host, drug combinations, reaction sensitivity and disease severity shall be taken into account. Administration can be carried out continuously or periodically within the maximum tolerated dose.

Unlike existing drugs, which often need to be taken daily for the rest of the patients life, a typical treatment relies upon a simple injection being administered by a doctor either weekly or monthly. A normal treatment programme is of three months duration, with an anticipated follow up procedure at six months, twelve months and two years or as necessary should the virus reappear.

The composition of the present invention may be used with other drugs to provide a combination therapy. The other drugs may form part of the same composition, or be provided as a separate composition for administration at the same time.

The invention also extends to a method of generation of a protective composition comprising reagent for use in protection of a non goat species, the method comprising immunising a goat with a non goat antigen (e.g. a virus or foreign protein), and purifying the serum extract produced in the goat after challenge with the antigen. The reagent may then be used to protect the non goat animal from the antigen used as immunogen.

The present invention further relates to use of a composition comprising the serum extract of a goat after challenge with a human HIV virus in medicine, and the use of a composition comprising the total antibody population of a goat after challenge with a human HIV virus in the preparation of a medicament.

Preferably, the composition of the present invention is treated by one or all of the following: precipitation with 45% ammonium sulfate, freezing at -70°C for 24 hours or microfiltration.

In one aspect, the product is preferably obtained from a goat which has been vaccinated against rabies.

In a variation, the present invention extends to product produced from horse, sheep and other suitable animals. The product can be obtained in a similar manner to that given for the goat product, and can optionally be assessed for anti-HLA and/or anti-FAS activities. In a further variation, the use of HIV virus as immunogen to give the product is not needed, and human white blood cells or human-derived cell-line-membrane antigens are employed as immunogen to give an effective antibody preparation. Furthermore, we envisage that antibody can be replaced by the immunogen, that is the therapeutic composition can comprise the HIV material or the white blood cells.

In yet another variation following heat inactivation a supernate solution upon which a viral culture has been grown or one which is capable of the same, but has not been used to grow a culture, may also be used as an immunogen which will produce a suitable response. Any supernate solution or other medium, which is suitable for the in vitro growth of HIV or another virus, may be used to produce an acceptable immunogen, which will produce an effective response. The supernate of a cell culture growth medium such as PMBC or the cancer immortal cell line as used to grow HIV 111b are given as an example. The HIV or other selected virus does not need to be present to produce an effective immunogen to create the preparation.

Without being bound by any theory, we believe that the presence of anti-HLA activity is an important constituent of the product of this invention. Preferably any antibody in the product of this invention is a polyclonal antibody that recognises a repertoire of HLA class II antigen and gp 120 antigen, or that recognises FAS. Our findings suggests that it is preferable to have HLA class II antigen. Notwithstanding our preference for anti-HLA activity, we do not eliminate the possibility that other active active molecules are present. In this respect, the compositions of this invention may therefore include an additional bioactive compound. We have already demonstrated that oral administration gives similar effects as injections. IgG should not cross into the blood stream

from the mouth, which lead one to believe that IgG may not be the only active component.

Suitable products can be raised by employing as immunogen a selection of antigens, preferably a cocktail of antigens. It is possible that the use of a range of different antigens give rise to antibody which recognises common structures of the antigens giving a stronger response in the patient. We hypothesise that a selection of HIV isolates will provide epitopes with minor variations in structure, and a pan-antibody will result.

Thus, to generate the serum, we prefer to employ a cocktail of different HIV viruses produced primarily in PBMCs, rather than use T-cells alone. The cocktail suitably contains 2, 3, 4, 5, 6 or more of such viruses. The viruses are preferably in the form of lysates, since lysates are non-infectious and serve to expose the immune system to internal proteins. Examples of preferred lysates include the following HIV-1 isolates: 91US056, 92HT593, 92US723, 92US657, 92US660 and 92US714. Preferably the cocktail includes at least 1, 2, 3, 4, 5 or all 6 of these particular isolates.

Thus, cocktails of similar cells can be employed (multiple PBMC donors, Multiple T Cell donors, Multiple activated Nerve cell donors). Multiple cell sources are expected to broaden the cellular protein range. This broadening might help alleviate differences in improvements one might expect with patents with different HLA types etc.

Cellular proteins are usually part of the active immunogen, such as , but not limited to FAS, IP10, NGFp75.

We envisage the use of different cell lines and types as immunogen source, in addition to H9 and PBMC. Other cell types that may express other proteins or similar proteins at a significantly higher level, thus altering the relative strength of the product, can be used. Antibodies to these different

proteins will work through a similar basic modulation mechanism. Ultimately, we might use this approach to improve the MS or nerve growth product by using activated nerve cells. This procedure can produce antibodies that inhibit the pathways that might concentrate on neural stress and damage, much better than the H9 lines which we are currently using. Similar considerations apply to activated bone cells on bone degeneration diseases.

Activation of cells, for example with Concanavalin A, can give advantages, and for example higher levels of anti-dopamine activity may be achieved using Con A. SHULA (non-activated) had no significant rise in the anti-dopamine R levels above baseline on O.D [where SHULA is an acronym for S's Human Leukocyte Antigens. It is considered non-activated. Activated cells have been stimulated to produce proteins. Though non-activated, the antibodies to cellular markers examined were strikingly similar with SHULA as with the HIV3B viral lysate, and the H9 cells alone, the cell line that the HIV 3B were grown on]. Meanwhile, the HIV 3B (averages of 12 goats and rabbit) did. There was also a rise in Dopamine R levels between the Con-A activated PBMC cells in the cocktail.

More generally, the present invention can employ inactivated cellular proteins. Some of the unknown proteins used to make antibodies of interest are found on both inactivated and activated cells (but most likely at different levels). An example of this effect was the amount of FAS found with the SHULA serum. With activated cells different activation methods can be employed.

In yet another variation a supernate solution suitable for the in vitro growth of the HIV virus but not limited to HIV will in the form of either PBMC or other medium such as an immortal cell line such as is used for example in order to grow HIV 111b will on its own without the introduction of the virus if heat killed in the normal manner used should the HIV virus not be present produce an effective antibody preparation.

Such preparations can also be obtained using proteins containing the peptides isolated from HIV lysates, synthetic peptides, synthetic oligopeptides, bacterial fusion proteins and proteins/peptides from phylogenetically unrelated sources which contain or mimic the desired cell culture or other supernate debris. Antibodies to lysate can be obtained and tested.

More generally, it appears that effective antibodies can be obtained using as immunogen, cells (or protein cocktail mixtures) that originate in a human. Antibodies from these human cells are then made in a host species, with the ultimate antibody product being used back in a human. The protein cocktail mixtures can be of extremely similar homology between the original donor and recipient. This homology allows the concept of proteins or cells of, for example, simian neural origins being able to work on a human. Highly conserved protein cocktails from a closely related animal are of interest.

It is also expected that there will be a relation between the HLA type of the person who donated the original cell, and the HLA type of the recipient. This relationship might explain some of the variability which has been seen, and can be taken into account when selecting a formulation for matching to a patient.

Furthermore, we envisage using activated or cancer cell lines from different parts of the body, including cell lines from neural blastomas, pancreas carcinomas, prostate and squamous cell carcinomas. Subtle differences between the antibodies created between these different cell types can be predicted to give a very different profile and might help target certain organ systems in a very broad sense.

There is some evidence that rabies vaccine given to the goats may be responsible for the observed therapeutic effect. We screened sera from goats obtained in Wales, including a pool of 3 different sera (normal sera) and from a

donor kid, which have not seen rabies or other preventative vaccines. These animals had no active antibody.

In yet another variation we envisage that cell membrane components shed during the propagation of cells in vitro may provide the antigens to which goat or other species may direct anti-body responses. This may occur in the absence of viral infection.

Without being bound by our current theory, it seems that the antibody of this invention acts to suppress cell proliferation of the kind which is required by HIV or other conditions reliant on such an immune response. Thus, for example, the present invention finds application in the treatment of multiple sclerosis.

Being aware from PCT/GB02/03037 of the possible significance of the anti-HLA and anti-FAS activity of the anti-body from the goat serum, it may be appropriate to assess the probable utility of a range of such goat sera. A simple assay can assess the presence of anti-HLA and/or anti-FAS activity, and permit identification of candidate serum suited for administration to patients.

According to the present invention, there is provided a method of preparing a serum, especially goat serum, which comprises administering one or more, preferably at least several, HIV isolates to the animal, allowing an immune response to develop, drawing blood from the animal, monitoring for the presence of anti-HLA antibody and/or anti-FAS antibody, and preparing an anti-HLA and/or anti-FAS serum suited for treatment of a human being.

Usually multiple animals will be employed, and the animals can be assessed for those which give the better yields of effective serum. Such better animals can then be bred to provide a lineage of animals especially suited for the present invention.

As well as palliative treatments, the antibody product of this invention is of use for the treatment of diseases with an inflammatory component, and includes not only HIV, but also diabetes, rheumatoid arthritis, neuritis, multiple myeloma, colorectal cancer, etc.

We have studied sera from different goats immunised with different virus/cell preparations and can show that cocktail injected goats produced an immune response which sees many of the cryptic i.e. silent parts of the HIV envelope, which may well be important.

Furthermore, this invention also provides methods of treatment of diseases using such products.

One method of the present invention is for treatment for diseases which include multiple sclerosis, rheumatoid arthritis, diabetes mellitus, primary biliary chirrosis, chirrosis autoimmune and viral b and c autoimmune conditions involving heart, lung, skin, gastrointestinal tract, kidney, brain, CNS. More generally, conditions which may be treated by the present invention include HIV, inflammatory diseases, autoimmune diseases, axonal or nerve damage or related impairment or cancers and other diseases or conditions with an inflammatory component.

The sera seems to be particularly suitable for diseases associated with chronically activated cells which may be secreting damaging messengers such as cytokines and chemokines. These include multiple sclerosis, all forms of chronic inflammatory conditions of the nervous system as well as of chronic infections such as viral, bacterial and tropical cancers associated with chronic inflammatory lesions, in particular those of the lung, pancreas, liver, bowel, lymph nodes, skin especially squamous cell and basal cell cancers may also benefit primary and secondary tumours of the brain and spinal cord.

The observed improvements in nervous function in those people with traumatic damaged nerves suggests a neuronal growth factor property and hence may be used for trauma, post infectious damage eg Guillian-Barre, malignancy damage etc, neuropathies associated with diabetes, alcoholism, poisoning with metals or other toxins etc.

Reports of reduced secondary cancer activity with the sera suggest direct anti-cancer activity.

In a particular aspect of this invention, the composition of this invention is employed both to provide palliative improvement in the condition of a patient and to treat a disease such as multiple sclerosis.

The recovery seen in many of the MS patients, alongside the elevated mood reported within the hour of receiving the treatment, has also prompted us to look for activity against receptors in the CNS which may be involved in nerve stimulation and possible regeneration. We have screened the various sera for activity against a number of antigens and have found activity against the dopamine receptor, serotonin receptor, Nerve growth factor receptor p75 and the chemokine CXCL10 (IP10).

Accordingly, the invention extends to antibody against one or more of the dopamine receptor, serotonin receptor, Nerve growth factor receptor p75 and the chemokine CXCL10 (IP10). One or more of these antibody activities may be present, alone or in combination with anti-HLA and/or anti-FAS activity.

The combination of anti-FAS and/or anti-HLA antibodies may be important, along with antibody against one or more of dopamine receptor, serotonin receptor, Nerve growth factor receptor p75 or chemokine CXCL10 and thus assays might be directed at the various antibody activities to ensure their presence in the product.

This invention also provides compositions containing antibody against one or more of dopamine receptor, serotonin receptor, Nerve growth factor receptor p75 or chemokine CXCL10, usually also with anti-FAS antibody and/or anti-HLA antibody, and methods of treatment using such combinations.

The anti class 2 polyclonal antibodies in this sera may work not only directly but indirectly. By the direct approach they would block the inappropriate presentation of peptides leading to the auto immune inflammatory destructive process.

The further mechanism is that by binding to class 2 on cells which would normally express the class 2 this may induce cell death of apoptosis. This is the same type of pathway which would be induced via the fas L network.

It has been reported that how cells die i.e.; by apoptosis or necrosis is crucially important as to the immune response to the antigens on the cells. In MS cell mediated immunity appears to be dominant over humeral immunity and treatments aimed at pushing the humeral or TH2 type of immune response are thought to be desirable in multiple-sclerosis. In the few patients we have examined for this activity before and after the administration of the serum they do indeed switch to the desired immune response. The desired immune response includes the inductional cytokines IL4, IL6, IL10.

Recent animal data suggests that animal models of MS can be improved with the induction of re-myelination using cytokines of the IL6 family which are part of the TH2 humeral path way.

The following points arise:

1. There is a strong position to claim that the inhibition of MHC class 2 polyclonal antibodies is probably able to induce more than one activity i.e. in as mentioned above one locking in appropriate presentation of self

peptides and hence blocking the paracrine drive which results in the de-myelination. (Paracrine meeting inducing responses from other cells which feed the damage).

2. Attaching to class 2 and inducing apoptosis of the cells either directly or by inducing antibody directed cytotoxicity of which there are multiple mechanisms.

3. By causing the cell death of the inflamed cells in such a way that they are taken up by antigen presenting cells and presented to the immune system in such a way that it shifts the immune bias to a TH 2 response which include the induction of IL6 responses which lead to the re-myelination of the de-myelenated plaques which are the hallmark of MS disease.4. The ability of class 2 to induce apoptosis on cell lines with inappropriate class 2 on mean that this treatment could be induced for those rare tumour types that hyper express MAC class 2. It has recently been shown that antibodies against these cell lines will induce apoptosis. We have noted increased apoptosis in some of our cell lines.

4. Several lymphomas and late stage melanomas express high levels of HLA class 2. Hence the polyclonal sera could be better treatment for these tumours than monoclonal therapies which are currently in development.

Several recent publications have emphasised the role of cytokines in driving the damage in MS. These include IL 1 and TGF beta which is alleged to increase a molecule called jagged 1 which appears to high in MS plaques and down regulates in re-myleninating lesions. 2. There is also considerable evidence that inflammatory cells exhibit resistance to apoptosis with higher expression of BCL2 and aflip proteins and that these are not affected by treatment with interferon beta. Induction of apoptotic pathways to circumvent the protective BCL2 pathway maybe an important component in the activity of the serum.

5. There is another route which has recently become more recognised as having potential importance and that is the claimed role for NHC molecules (HLA in human) in the development of the nervous system. This works which at first appears to defy both immunological and neurological dogma shows how MHC molecules present on brain tissue determine how the brain tissue interacts with its environment and regulates neural development especially of the eye. Inappropriate HLA expression when locked may explain the rapid re-organisation and re-myelination seen in some of these patients who have had visual improvement following extant visual impairment of several years standing.

6. These observations include those previously made for HIV which is non-specific and could be used for the treatment of any chronic infectious disease. This can probably be the down-regulation of the chronic inflammatory processes.

7. A dramatic improvement in severe gout has been noted following the administration of serum. A dramatic improvement in wellness and increase in energy levels have been noted by most of these patients.

8. An improvement in two patients with Parkinson's disease. This may either be due to the induction of the necessary transmission factors or maybe due to it anti-inflammatory effect on an agent driving the disease. (chronic helicobater infection has been postulated).

9. There has been a marked effect on patients with carototic lesions and both early squama cell carcinomas and basil cell carcinomas have been resolved on this treatment. This is extremely unlikely to ever happen without active treatment. It therefore transpires the serum acts directly

or indirectly by inducing various cytokines/chemochines etc. which lead to the induction of apoptosis and resolution of these skin lesions.

10. The induction of a nerve growth factor re-myelinating factor is important in its own right as two patient's have had regeneration of traumatic of nerve severation nothing to do with there MS. This is encompassed scientifically again either by direct activity or the indirect induction of the afore said growth factors including IL6. Although it is possible to explain many of the features above by either direct or indirect responses to the administration goat serum with anti-DR antibodies (and the DR aspect is probably extremely important as opposed to other class 2 types in general as these inhibit the next lymphocyte responses which the goat inoculating goat serum does incredibly well, with other anti class 2 antibody responses not been nearly efficient).

It is also possible that there is another very important agent apart for other antibodies, and known anti inflammatory targets previously mentioned including fassil and Icam.

Beneficial effects may well be caused by a molecule or antibody induced by the inoculation vaccination process.

The fact that there must be some such antibody is rendered more likely by the fact that all patients experience a feeling of extreme well being within 15 mins of the first injection. This is lead to anorexic people suddenly craving a powerful appetite and this function could therefore be useful for anorexics and cocexic people with cancer.

A cardinal feature of MS lesions is the inappropriate expression of HLA-DR on neuronal cells including astrocytes (Traugott and Lebon, J.Neurol 1988 April 84 257 and Microglia J.Neurol Science 1987 August 80 25-37). It is thought that this inappropriate expression presents self-neuronal antigens to the

immune system and also acts as a target. Cells expressing inappropriate Class II are associated with a classic ongoing inflammatory response. Anti-inflammatory treatment per se is well known to dramatically improve the relapsing remitting type of MS. More recently it has been shown that the resulting products of inflammation such as cytokine and chemokines may be responsible for the neuronal damage and demyelination in particular. In a recent mouse virus model of a chronic demyelinating disease it was shown that neutralisation of the chemokine CXCL10 reduced the inflammatory cell invasion demeylination and actually improved neurological function. The model showed a pronounced suppression of ongoing demeylination which was associated with improved neurological function. This was associated with marked remyelination. Thus observations in both classic laboratory models as well as our own suggest that the damage seen in multiple sclerosis may not be as acute and permanent as the clinical features of secondary progressive Ms suggest and that the chronic inflammatory state is akin to shorting out the eurological system as opposed to permanently damaging it, at least in the early phases.

The inflammatory cascade is associated with high gamma interferon levels which are thought to lead to the inappropriate up regulating of HLA Class II on neurological tissue as well as marked inflammatory response leading to multiple cytokine and chemokine affects. Further studies on this sera have shown that it has activity against at least 3 different inflammatory pathways. Moreover, all patients treated to date who have been able to provide sera before and after treatment have shown a reduction in gamma interferon and an increase in TH2 cytokine production which is the desired immunological effect of an ideal immunotherapy.

There is yet another pathway that needs to be considered, and that are the downstream immunomodulatiory effects evoked by triggering certain HLA class II molecules and inter-related complexes on the surface of certain APC populations. Thus, apart from physical loss of the offending APCs by apoptotic

removal we may actually be triggering anti-inflammatory cytokines and regeneratory growth and repair factors.

The goats are likely producing a factor on the surface of a human lymphoma cell line which has changed its phenotype when infected with this deceptive foe (HIV). Indeed, in addition to induction of xeno-type responses in goats to everything foreign on thee human lymphoma cells, these cells have also unregulated certain molecules (danger-like ligands) in response to presence of HIV in these cells.

We treat patients very successfully with vision problems when they occur as part of the general debility problems associated with multiple sclerosis. Not all patients get this problem, but in those that do, it usually disappears within a few days, (i.e.) they get their vision back.

The same type of visual problem seems also to occur in patients who do not have MS.

In the opening public lecture of the 32nd annual meeting of the Society for Neuroscience on how histocompatibility builds the brain Investigator, Carla Shatz not only described how the visual system is established, she discussed her latest revelation: Molecules best known in immune recognition are involved in building the neural connection system.

Many scientists liken neural connections in the brain to their electrical counterparts in a computer. But Shatz, who specializes at Harvard Medical School in the development of mammalian visual systems, showed that connections in the mammalian brain are much more flexible than the hardwired links in computer chips.

During eye development, signals are relayed from the retina to the lateral geniculate nucleus (LGN), and then on to the visual cortex of the brain, where

the information is processed. Initially the connections from one eye are randomly intermixed with those from the other eye in the LGN and at the cortex. But early in development – before the eye even opens or functions – neighbouring groups of retinal neurons fire in waves, without any input signal. These waves of autoimpluses from the neighbouring retinal neurons seem to strengthen some connections in the LGN and cortex, while weakening others.

The end result is that the signals from one eye are interspersed in a layered pattern with inputs from the other. Like the black and white stripes of a zebra, the stripes of input from each eye are juxtaposed, but not intermixed, in the mature brain.

Shatz's group has shown previously that if they block the autoimpulses from the retina to the LGN, then the neat layering of the normal adult pattern fails to form, and the immature intermixed pattern remains. Thus the researchers conclude that the adult pattern is the result of simultaneous weakening of some connections and reinforcement of others. But the exact molecules involved in the process have remained largely unknown.

Now Shatz and colleagues have made the surprising discovery that proteins in the major histocompatibility complex class I (MHCI) are directly involved in the process. Previously, MHC molecules were thought to be in the sole purview of the immune system, where they are responsible for presenting foreign antigens to E-cells and inducing cellular immune response. But when Shatz's group used microarrays to compare mRNA from LGN neurons that had normal inputs from the retina to ones that had the connections blocked, they found the MHCI RNA was present only in the normal LGN.

Shatz's group also has light microscope data indicating that the MHCI proteins are present at the synapse in several regions of both the developing brain and the adult brain.

Her current hypothesis is that the MHCI proteins are the "anti-glue" that allows the inappropriate early connections to be broken down. Imagine the MHC1 protein sitting on the in the membrane of the post-synaptic neuron, she suggests, and interacting with a protein complex on the presynaptic neuron. Shatz speculates that the interaction initiates a signalling cascade that somehow reduces the strength of the connection, eventually leading to its complete elimination.

EXAMPLES

Palliative Treatment

Upon administration of the composition, we have noted the following improvements in the health and condition of patients:-

1. Skin
   Skin tones up; has somewhat younger appearance; more youthful; skin tags disappear; wounds heal more quickly (including dental work to gums) thread veins disappear; there seems to be improved vascular circulation (possible alleviation of haemeroids).

2. Nail Growth
   Fingernails and toenails grow more quickly and grow more strongly.

3. Hair
   Grows more quickly; hair is softer and shines; a head of hair is fuller; possibly some re-growth where hair loss has occurred.

4. Muscle Tone
   General improvements; sufferers from back pains have found relief.

5. Memory and Co-ordination

General improvements.

6. Well Being

Clear feeling of well-being; increased energy levels; anti-depressant effect noted.

7. Appetite

Considerably increased.

8. Sexual Activity

For both sexes, increased libido. For males: restoration of erectile function; increase in seminal fluid. For females: improved lubrication

Thus, in a preferred aspect, the present invention provides a method for improving one or more of the factors (1) to (8).

Treatment of Disease

Patients (who are under self-administered treatment and/or supervision from their doctor and/or treatment overseas) have taken the treatment by subcutaneous injection. The number of patients is shown in brackets.

The conditions they are suffering from, and the observations that have been made, are as follows:-

1. Cancer and Growths (8/9).

For terminally ill patients, increased life beyond the prognosis given by their hospital or doctor.
Melanomas and certain other skin pre-cancers disappear.
Sebaceous and Other Cysts. They disappear.

Reduction in fibroids (female)

Patient AAA (male). A former PT instructor in the Royal Marines with throat cancer (one effect of which was impaired speech). He is now free from this condition. He has resumed his daily fitness programme (particularly bench press-ups) more actively than when he was in the Marines.

Patient BBB (female). With uterine polyps. Now free of this condition.

Patient CCC (male). Rodent ulcer/weeping sore. Now free of this condition.

2. AIDS/HIV (100+)
   Maintained health levels. Absence of secondary infections (colds, thrush etc.)

3. Multiple Sclerosis (30)
   This is the most closely observed group and, apart from the AIDS/HIV patients, it is the largest in number. All have felt the improvements in condition listed in (A) above. There is increased mobility, improved co-ordination and an improved ability to 'look after oneself', with less dependence on care assistances.

   Patients whose deteriorated condition had led to impaired bladder function and bowel movements, report a significant restoration of normal functioning to bladder and bowel.

4. Motor Neurone disease/ALS/Muscular Dystrophy (1)
   Improved mobility and co-ordination.

5. Gout (1-3).

There is one principal patient, but two other patients being treated for other conditions have reported positively on their previous intermittent gout attacks.

6. Parkinson's Disease (3)
   Improved co-ordination.

7. Rheumatoid Arthritis and other Bone/Joint Ailments (1)
   The patient reports no recurrent attacks of rheumatoid arthritis and an absence of inflammation.

   In other patients there is evidence of reduction in osteoarthritic nodes and, in the case of osteoporosis, increased bone density.

8. Bone and Nerve Re-Growth (2)
   Observational evidence seems to imply some re-growth, repair, or partial re-connection for two patients.
   Patient DDD Lamenectomy. Severe damage to 1 vertebra. Used to walk with sticks and needed a wheel-chair to board aircraft. Had pain and movement was limited. Now mobile and pain-free

   Patient EEE An MS sufferer. Has observed return of 'feeling' in nose and a damaged finger.

   A third patient's condition of stenosis was relieved.

9. Eye Sight / Neural Connection Systems
   The treatment appears to have been effective in removing cataracts in two patients. A number of MS patients with retinal atrophy have experienced significant restoration of eyesight which was either failing or, in the case of one patient, which had been blindness over number of years.

10. Diabetes

A patient with Type 2 diabetes has reported that their blood sugar levels have returned to normal.

11. Inflammatory Relief

The treatment appears to give relief for a number of inflammatory conditions. This is a common observation in the broad range of conditions described above, and in the specific illnesses described below. There is no collected data for asthma (being inflammation of the lung tissue) but one patient may be showing some relief of this condition. A number of heavy cigarette smokers may also be experiencing easier breathing.

Treatment of non-human animals

There has been no programme to treat animals. However, four patients have given the treatment orally to old and sick domestic pets. All four report the same improvements in condition observed in humans.

Case 1 Dog. Age about 11 years. Condition: Cancer/pain

Result: Relief of pain; some extension of life.

Case 2 Dog. Age about 15 years. Condition: Arthritic joints; severely impaired walking.

Result: Greatly increased mobility. Reduction in panting (being a sign of pain).

Case 3 Dog. Age unknown. Condition: Arthritic joints; pain.

Result: Greatly increased mobility.

Case 4 Cat. Age about 17 years. Condition: Emaciated body; poor coat of fur.

Result: Return of coat quality and appetite.

Examples of Comments from Patients

Patient ZZ

After having MS for 27 years this November I felt there would be a cure on the horizon but I felt I would not see it in my lifetime. I just thought that I would see it but only for a few new babies that would be vaccinated against it like Polio etc. that was my feelings anyway. Last October when some friends phoned me and told me they were able to get me this programme I was thrilled, I thought my prayers had been answered.

Even after the very first injection when I had amazing results my eyesight had begun to improve after a few minutes, and the doctor and another person who were sitting in the surgery with myself and my husband thought it was amazing too.

After that I went from strength to strength, my walking was fantastic and around the house I didn't have to use my stick or in the few weeks previous a walking frame that the hospital had loaned me. My wheelchair had become redundant expect when we went for longer walks.

Even after my husband and I had caught one of those nasty viruses which knocked us for six, in fact he even passed out and hit his head on the radiator which left a nasty bruise on his forehead, I was just unable to walk anywhere without help of some sort. This all happened last January and other than felling weak for a while I picked up very quickly. I do fell though that if it wasn't for this treatment I would have had a relapse and been very poorly and maybe even sent to hospital and been on steroids just like I had in the past after things like this happened to me.

As time went on we did have a couple of blips, but nothing I couldn't cope with as I knew what this treatment could do for me in the future. I have even been asked to talk on the phone to others who are considering starting this treatment and I am still in contact with them now, so we know how we are doing and once again when they maybe having blips I can tell them not to worry as it turns out OK and to stay with it. I can honestly say hand on heart that this treatment has given me back a marvellous quality of life that I thought I had lost, it is truly the light at the end of the tunnel come true for me and for many other and I could go on and on about it but there is not enough hours in a day to do it justice as far as I'm concerned. Thank you for finding time to read this.

Patient YY

Since taking medication, small, but clear improvements have occurred:

- The right eye, which up to then had been static, moves again
- Bladder weakness has almost gone
- I feel I have more energy, and tiredness during the day has decreased
- Balance has become much better, but sill unsteady
- I can stand up straight again and do not rock
- I can use both legs again when going upstairs; always going up, and often when coming down.

There is no improvement in style when walking, but there is an improvement in duration; distances are slowly getting longer.

Note: I have only been taking medicine for a short period: the first injection was made 11 weeks ago.

Patient XX

I have been using the new animal serum since 21/03/02. I have been diagnosed with MS and the only therapy available to me up to now is Avonex Interferon beta-la. The Interferon certainly has no visible effects on my

condition which has progressed to difficulty in the gait, a stiffness in my legs, problems with urgency and frequency of urination and difficulties with the bowel.

From my very first application of this serum, I discarded my stick which I very rarely us now, the problems with the urgency and frequency have all but disappeared and although my gait has not noticeably improved my general sprits have because I genuinely feel that it has made a great and positive difference in my symptomatic picture. I am a firm believer in this line of approach to this disagreeable illness and I urge all concerned people to please take note of its helpful and dramatic effects.

Patient WW

Between December 2000 and 2002 I have been in hospital and rehabilitation 6 times due to MS attacks, my problems were dizziness, loss of balance, tingles in my feet, legs hands and back. Patchy numbness in my feet, legs, arm and face, stiffness in my legs, twitching inside the right hand side of my face and in both eyes. A pulling sensation in my head and not being able to walk properly, sometimes my walking was reduced to just a few steps, I had no energy and suffered very badly from depression, was always sleeping and had no interest in anything – I had nothing positive to hold onto. These are just the problems I have had since December 2000.

June 19th 2002 changed my life around, I had my first injection of the serum, since then I have never looked back. The tingles and the patchy numbness is reduced, I still have the tingles in my right foot but not at all like it used to be. My balance is much better and I have so much energy now and I don't sleep like I use to.

My right pupil which has dilated since the diagnosis of Optic Neuritis in 1986 is now the same size as the left pupil. 6 weeks ago I actually made my son's bed and I'm starting to do small jobs around my flat. I went shopping 2

weeks ago, it was the first time in may months and I stood in the supermarket for nearly 2 hours, I haven't done that for nearly 2 years. I now go swimming which wasn't possible before due to the weakness in my legs, and I meet regularly with friends, I still have my bad days but they are becoming fewer as the weeks go by.

Since I have been taking the serum it has given me back my life, dignity and self esteem and my children back their mother.

My physiotherapist has said my legs are approx 15% stronger and that's after just 6 weeks.

Patient VV

I am 44 years old. I am married and have three wonderful children.

I was officially diagnosed with multiple sclerosis three years ago. I say officially as along with most fellow sufferers, the realisation of one's symptoms and condition brings with it the realisation that indeed these symptoms were preset for quite a while but just thought that you had been dumsy and under the weather.

In fact my symptoms were classed as many weird and wonderful thins including the menopause. I cannot put all the blame on those who should know as the information regarding this illness and the lack of things to treat it with cause problems. I did try intaferon, it didn't work for me.

Anyway by the time I had been diagnosed things started to progress. Two years ago I was at the point of despair. Spasms in my legs, I dragged my right leg and would pull it along using my left hand, as my right hand was getting unusable. I dropped everything I tried to grab or reach for. I became increasingly disorientated falling over all the time if I was unaided. My memory was not functioning properly in mid flow of conversation the words would leave

me, frustrating and embarrassing. I had to be reminded of the most simplistic things, and worst of all I had misplaced my memories of precious gems, one being those of my children's baby day's and most of their growing years. My speech then followed and I have periods of not being able to communicate properly.

My appetite diminished and sleep although badly needed as exhaustion was incredible and I had no choice but to take to bed ruing the day sometimes nearly all day, was sometimes a nightmare because the spasms would wake me up, and so too my husband in the night.

My eyesight had begun to give problems, I had previously never suffered in this way. My bladder was very badly effected and so too my bowels. Life had changed dramatically not for good; I became and was beginning to take on the life of a recluse because to attempt to go out was a nightmare. If it was a public place ie, a restaurant, cinema etc there would have to be a sweep of the intended destination to see where the toilets were, if it had steps in the building to negotiate, how many and what facilities were there for people like me, and believe me there weren't many, also that at a moment notice I might have to cancel because I was not strong enough to attend.

Life was bad and for my family as well because they were victim too of this beast within. I couldn't participate in the normal parent children things, and the children were worried sick. We had no future and couldn't plan one because I was spiralling downwards. It affected our marriage and I began to realise that it could possible that I wouldn't be around for my children, that really hurt. Also the fact that I was not going to get better because there was nothing that could help, and so faced with this, started planning my way to eventually ending up in residential care my choice, as I had lost myself and making choices in life, the beast was taking over and my last and only choice would be one of dignity.

Then I came across this Gift of Life, and embarked upon the next journey of life which to be honest when told about it thought well I have nothing to lose and it didn't take me long to agree to try.

This came to be the best decision ever, I started receiving the injections and could arise out of a chair from sitting position straightway rather shakily, impossible usually. In fact I basically crawled in and came out waling. I was thrilled, and wept with tears of complete joy. I continued the injections and every week a new revelation within my body and the restoration of things that had been torn away from me.

And now two years later I can walk perfectly well, my speech is fine my co-ordination is great, my bladder I have no problems with so too my bowels, I eat well and my memory has begun to filter back both short term, and long term. Well I am reclaiming my treasured gems and am beginning to have a mental full diary of my children's past

My stamina is now very good and so are my energy levels. I in fact look after my parents my father being rendered disable 1 year ago, my mother does not keep the best of health either so I run tow households now and find time for some voluntary work.

See without this wonderful medicine I dread to think where I would have been now, if here at all. I have been given my life back, and so have my family. The children have been given their mother back to them and my husband has now got his wife back. We can and do plan our future as now even feel that now we do have one. I never dreamt in a million years that this was possible but it is and I'm living proof. I have been given the Gift of Life.

Fairy tales do come true and we will live happily ever after.

Patient UU

Please find some observations I have noticed with only modes use of the 1gG. For the record, the most I have ever taken is 2.5 mg on a 4 week cycle.

Concrete items that I can give specific details include:

First and foremost the carototic lesions below my eyes are under control. Aside from scientific curiosity, this was the prime personal reason for trying the IgG. I spent the better part of a decade in an outside environment with much exposure to the sun. As a result, I have had significant scaling and redness below both eyes for a number of years. Creams and lotions would temper the situation, but it was always red. At the same time, my facial skin is supple. Body skin does not feel as "dry" as it should for this time of the year. Lotion is not required on my shoulders on a daily basis as before. I currently still apply lotions to the skin, but not significantly different than I have for the past four or five years.

I have not had a significant cold in over a year despite – 12 trips to the UK from the USA, and coming home to kids in school. This may be just good luck, or good living, but I would have expected a real "knock down" type of germ. Please note that I have had a number of "near misses", but no direct hits.

I have not needed coal tar based shampoo to control dandruff in months. Usually, this would be a daily requirement, especially in the months between October-April. Even with the coal tar based shampoo treatment, I would have an itchy scalp within 24 hours. Now I am using a milder shampoo this November. Furthermore, if I miss a day, I do not feel the "itch" like I would have previously.

There is more prostate fluid being manufactured. Speaking of the urinary area, I have noticed that there are fewer "lingering" drips after urinations. The speed of shutting off the urine stream is much closer to what it

was when I was 20-30. I noticed this shutting off process slowed down about 6-7 years ago.

I find there is no more morning "stiffness". There is no minute or two needed to "limber up".

Less concrete observations:

I notice that I just seems to have more "energy" and more alert. This is not like having an extra cup or two coffee; it just seems that I can concentrate better.

There is also a general feeling of "well being". This is not like being intoxicated. It is more like how once feels after a "really" good night sleep.

A final area where I notice improvement, but have problems documenting a "before and after" is my muscle tone. I seem to be able to retain muscle tone longer. For example, I did not run in the morning during my last trip to the UK. I normally get out at lest 2 mornings for a run... This gave me a 10 day lag between morning runs. Upon my return, I felt no stain on my first run and actually got a "runners high". The runners high should have taken at least one or two more AM runs to attain again.

My eight year old Border collie (sheepdog) Taran has hip displasia and currently takes 150mg rimadly to relieve discomfort in his hips. Being a working border collie that I personally trained, we have an understanding of each other that is much more intense than a traditional dog/human relation. In order for us to work the animals together, we both need to know exactly what the other is thinking. On Wednesday, Nov. 19, he received 15 mg orally of the 1gG. I could tell that he got the immediate "feeling" of well being as he stayed in my office next to my chair for an hour or so with a slightly different expression. Three days later, I notice that he is twisting his upper body and spinning much

more when playing with our younger dog. He is also following me around the house much more as opposed to lying on his heated mattress. His facial expressions were that of a younger and "happier dog".

I am unable to tell if it is actually helping his hip significantly, but is seems to be helping with other aliments like stiffness which I was unaware he was feeling. There also seemed to be a general feeling of well being. I plan to give another 1.5 mg this upcoming week to see if my initial impressions continue.

Further Patients

A patient who had suffered from progressive multiple sclerosis for 3 years volunteered to try the serum. In short, she had a marked clinical improvement which is maintained over 6 months since commencing the treatment. Objective improvement was reported in at least two other patients. As fellow MS sufferers learnt of the improvement they requested access to treatment. Prior to treatment it was recommended that a formal functional assessment should be carried out by neurologists and that this be repeated one month later. Several of these patients were also seen by a local doctor who also documented their progress.

The doctor has reported that all except one patient has had a marked clinical improvement following this treatment. Much of this improvement relates to a feeling of well being, increased energy levels and improved subjective sensory reports. A neurologist has confirmed that at least two of these patients have had significant objective responses which are unexpected in this group of patients and which cannot be put down as a placebo.

In addition, this group of patients have confirmed the total lack of any serum sickness or other significant side effect bar the red, inflamed and sometimes

itchy response at the site of the subcutaneous injection which is never more than 1ml in volume.

Claims

1. A method for palliative improvement in the condition of a human or non-human animal, which comprises administering a composition containing anti-HLA antibody.

2. A method for palliative improvement in the condition of a human or non-human animal, which comprises administering a serum composition obtained from a goat after challenge with HIV.

3. A method according to claim 2, wherein the goat is immunised with an HIV lysate.

4. A method according to any preceding claim, which improves one or more of skin, nails, hair, muscles, memory, co-ordination, energy, depression, appetite and sexual activity.

5. A method according to any preceding claim, wherein the animal is being treated for a disease by administration of the composition.

6. A method according to any of claims 1 to 4, wherein the animal is not being treated for a disease.

7. A method according to any preceding claim with multiple administrations of the composition.

8. A method according to claim 7 with at least five administrations of the composition.

9. A method according to claim or 87, with weekly or monthly intervals between the administrations.

10. A process for preparing a pharmaceutical composition, which comprises injecting a goat with a cocktail of HIV lysates, preparing an extract of serum from the goat, and checking for the presence of one or more selected antibodies which is not anti-HIV antibody.

11. A process according to claim 10, wherein the selected antibody is chosen from anti-HLA, anti-FAS, anti-dopamine receptor, anti-serotonin receptor, anti-Nerve growth factor receptor p75 and anti-CXCL10.

12. A process for preparing a pharmaceutical composition, which comprises injecting a goat with a cocktail of HIV lysates, preparing an extract of serum from the goat, and testing for the absence of anti-HIV neutralising antibody.

13. A process for preparing a pharmaceutical composition, which comprises injecting a goat with a cocktail of HIV lysates, preparing an extract of serum from the goat, and testing for activity in palliating the condition of an animal.

14. A process for identifying a drug, which comprises injecting a goat with a cocktail of HIV lysates, preparing an extract of serum from the goat, and isolating a molecule responsible for activity in palliating the condition of an animal.

15. A process for identifying a drug, which comprises injecting a goat with a cocktail of HIV lysates, preparing an extract of serum from the goat, and isolating a molecule responsible for activity in the treatment of disease with an inflammatory component.

16. A process according to claim 14 or 15, where the molecule is selected from a cytokine, hormone, or other bioligically active goat molecule.

17. A molecule identified by the process of claim 16.

18. A pharmaceutical composition containing a molecule of claim 16.

19. A pharmaceutical composition containing as an active ingredient an extract obtainable by a process of administering HIV to a goat, and preparing an extract of serum of the goat.

ANNEX II

Fisher, Sally

From: Kirsty Stephens (DHL GB) [Kirsty.Stephens@dhl.com]
Sent: 23 August 2010 14:14
To: Fisher, Sally
Subject: FW: awb 7866012416

Hi Sally

Please find below requested proof of delivery

Delivery date:	20.08.2010	Service Center:	AMS-DHX	Courier Route ID:	L130.C	Courier ID:	

Delivery sheet

	Consignee	P	AWB / Pcs	ORG	Instruction	Pcs	Weight PU Date	Charge	Time	CP	Print Name
1	J VAN VLIET VRIJBURGSTRAAT 21	S	1567412276 (J) JD01 3029 5794 0007 3422	HKG		1 /1	4.5 17.08.2010		9:50		J. VAN VLIET
2	Dr Jonathan Heeney Vrijburgstraat 25	U	7866012416 (J) JD01 3043 8831 5038 3628	CBG		1 /1	2.6 16.08.2010		10:18		J. Heeney
3	APEX B.V. WESTEINDE 26/A	U	1940009805 (J) JD00 1304 1449 4200 1218 0	ROM		1 /1	0.5 19.08.2010		9:54		Hugas

Regards

Kirsty Stephens ext 6836
Service First Tracing Agent

23/08/2010

DHL International (UK) Ltd
Millennium House
Unit 5, Argosy Road
East Midlands Airport
Castle Donington
DE74 2SA
United Kingdom
tel: 0844 248 0800
Email: kirsty.stephens@dhl.com
www.dhl.co.uk

Please consider your environmental responsibility -*Do you **REALLY NEED** to print*

Williams, Andrea

From: Fisher, Sally
Sent: 20 August 2010 14:22
To: Fisher, Sally
Subject: Emailing: DHL Corporate - Package Tracking Results.htm

From: Subject: DHL: Corporate - Package Tracking Results Date: Fri, 20 Aug 2010 14:19:00 +0100 MIME-Version: 1.0 Content-Type: multipart/related; type="text/html"; boundary="----=_NextPart_000_0000_01CB4072.A24C2620" X-MimeOLE: Produced By Microsoft MimeOLE V6.00.2900.2962 This is a multi-part message in MIME format. ------=_NextPart_000_0000_01CB4072.A24C2620 Content-Type: text/html; charset="iso-8859-1" Content-Transfer-Encoding: quoted-printable Content-Location: http://www.dhl.com/cgi-bin/tracking.pl?docheck=1&TID=CP_ENG&AWB=7866012416

These are the results of your=20 query

Times given = are local to=20 the service area in which the shipment checkpoint is=20 recorded

Airwaybill=20 Number	Origin Service Area	Destination Service Area	Status
7866012416	Cambridge - = UK	Amsterdam - Netherlands,=20 The	Signed for by: HEEL = V Shipment delivered August 20, 2010 08:57

7866012416 - Detailed = Report

Date	Time	Location Service=20 Area	Checkpoint=20 Details
August 18,=20 2010	15:02	Cambridge -=20 UK	Shipment picked=20 up
August 18,=20 2010	16:43	Cambridge -=20 UK	Processed at=20 Cambridge - UK
August 18,=20 2010	17:57	Cambridge -=20 UK	Departed from DHL=20 facility in Cambridge - UK
August 18,=20 2010	19:39	East Midlands -=20 UK	Arrived at DHL=20 facility in East Midlands - UK
August 18,=20 2010	20:47	East Midlands -=20 UK	Processed at East=20 Midlands - UK
August 18,=20 2010	21:12	East Midlands -=20 UK	Departed from DHL=20 facility in East Midlands - UK
August 18,=20 2010	21:22	East Midlands -=20 UK	Arrived at DHL=20 facility in East Midlands - UK
August 18,=20 2010	21:51	East Midlands -=20 UK	Processed at East=20 Midlands - UK
August 18,=20 2010	23:08	East Midlands -=20 UK	Departed from DHL=20 facility in East Midlands - UK
August 19,=20 2010	01:37	Brussels -=20 Belgium	Arrived at DHL=20 facility in Brussels - Belgium

August 19,=20 2010	03:03	Brussels -=20 Belgium	Processed at=20 Brussels - Belgium
August 19,=20 2010	04:34	Brussels -=20 Belgium	Departed from DHL=20 facility in Brussels - Belgium
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August 19,=20 2010	09:25	Amsterdam -=20 Netherlands, The	Delivery=20 attempted; recipient not home
August 20,=20 2010	08:14	Amsterdam -=20 Netherlands, The	With delivery=20 courier
August 20,=20 2010	08:57	Amsterdam -=20 Netherlands, The	Shipment=20 delivered

------=_NextPart_000_0000_01CB4072.A24C2620 Content-Type: application/octet-stream Content-Transfer-Encoding: base64 Content-Location: http://www.dhl.com/art/del.gif
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zcml6opAkQFgUwMm9AzUiZjfm6vbeGSIAgAh/hRnaWZ3aXphcmQuY29tIEd1ZXN0AAA7 ------
=_NextPart_000_0000_01CB4072.A24C2620--

ANNEX III

HGF LAW
Specialists in Intellectual Property

Marks & Clerk
62-68 Hills Road
CAMBRIDGE
CB2 1LA

RECEIVED
19 JUN 2008

18 June 2008

Your ref: GOW/aw/USP284207
Our ref: MJF/Q117436

Dear Sirs

US Patent Application No: 10/482399
In the name of AIMSCO Limited

We refer to your letter of 10 June 2008. We act for Jonathan Heeney. Our client's position was made clear in our letter to your client's solicitor on 5 April 2007. For the record, Mr Heeney's correspondence address is his address in the Netherlands and not at the University of Cambridge. We see no need for further correspondence on this issue but any such correspondence should be directed to us and not to Mr Heeney in any event.

Yours faithfully

HGF Law
HGF LAW

ANNEX IV

HGF LAW
Specialists in Intellectual Property

Matthew Arnold & Baldwin
21 Station Road
Watford
Herts
WD17 1HT

5 April 2007

Your ref: RDG.mxb.44658.12
Our ref: MJF/Q117436

BY POST AND FAX: 01923 216050

Dear Sirs

Aimsco Limited

We act for Professor Jonathan Heeney in his private capacity in relation to Patent Application number PCT/GB02/03037.

We refer to your letter to our client dated 26 March 2007. You have not indicated the basis upon which our client should sign the Declaration for PCT Application.

Our client will be prepared to sign the Declaration on the basis that all monies owed to our client are paid (as detailed in the enclosed document) and on the basis that all claims against Professor Heeney including those in the Daval International Limited v Argyll & Ors are withdrawn and that your client agrees to pay his costs to date in relation to the action.

Yours faithfully

HGF Law

HGF LAW

A-1

Daval International Ltd (Formerly Davis-Daval)

Consultancy payments outstanding to Dr J.L. Heeney

Based on £140,000.00 per year as agreed with Mr DJ Shotton, after he neglected to pay itemised bills for consulting in 2001 and 2002.

Jan. 2001	unpaid	(owing £11,500/month)	
Feb. 2001	unpaid		
Mar. 2001	unpaid		
Apr. 2001	unpaid		
May. 2001	unpaid		
June. 2001	unpaid	(Heads of agreement signed)	
July. 2001	unpaid		
Aug. 2001	unpaid		
Sept. 2001	unpaid		
Oct. 2001	unpaid		
Nov. 2001	paid	Dec 21st, 2001	£11,495.57
Dec. 2001	paid	Jan 14th, 2001	£11,495.57
Jan. 2002	paid }	paid on Feb 20th, 2002	
Feb. 2002	paid }	Feb 20th	£32,307.69
Mar. 2002	paid }	paid on Feb 20th, 2002	
Apr. 2002	unpaid		
May. 2002	unpaid		
June. 2002	unpaid		
July. 2002	unpaid		
Aug. 2002	unpaid		
Sept. 2002	unpaid		
Oct. 2002	unpaid		
Nov. 2002	unpaid		
Dec. 2002	unpaid		
Jan. 2003	unpaid		
Feb. 2003	unpaid		
Mar. 2003	unpaid		
Apr. 2003	paid in part on April 30th '03		£15,000.00
May. 2003	paid in part on June 5th '03		£10,000.00
June. 2003	unpaid		
July. 2003	unpaid		